

REMARKS**1. STATUS OF THE CLAIMS**

Claims 23-42 are pending.

Claim 23 has been amended by replacing “an Arabidopsis nucleic acid sequence encoding an amino acid sequence for an Ftn2 protein” with “SEQ ID NO:3.”

Claim 31 has been amended to avoid potential prolixity by replacing “wherein said amino acid sequence comprises” with the term “that comprises.”

Claims 35-42 were withdrawn by the Examiner for allegedly being directed to a non-elected invention.

Independent Claims 43 and 51 have been added to recite particular embodiments of the invention. Support for the recited ranges of identity to SEQ ID NO:2 in (a) to (c) are in the specification that teaches:

“An Ftn2 polypeptide is a protein (about 660 to about 800 amino acids long) which can be roughly defined by three regions. The N-terminal (about 420 amino acids) contains the DnaJ-like domain, and exhibits a high degree of homology among Ftn2 proteins obtained from different sources (**about 20 to about 60% identity**, and about 50 to about 80% similarity). The large central region (about 200 amino acids) is fairly variable, and exhibits a lower degree of homology among the different Ftn2 proteins (**about 6% to about 20% identity**, and about 20 to about 44% similarity). The C-terminal region (about 110 amino acids) is more highly conserved and in Arabidopsis Ftn2, contains putative myb domain (residues 677-690). The C-terminal region exhibits a higher degree of homology than the central region (**about 15% to about 55% identity**, and about 40 to about 70% similarity). The result is that when considered as a whole, homologous Ftn2 proteins possess about 15% or greater identity and about 38% or greater similarity to AtFtn2 protein. However, the N-terminal and C-terminal regions possess a higher degree of similarity and a higher degree of identity among the different Ftn2 proteins than do the whole proteins.”¹

Support for the recitation that “decreasing the amount of said encoded amino acid sequence” in the cells comprising a plastid (Claim 43) and the prokaryote cell (Claim 51) results in incomplete division or no division of the plastid and prokaryote cell is in the Specification’s teaching that:

“An Ftn2 polypeptide functions in prokaryotic-type division, such that a decreased amount of Ftn2 polypeptide in a prokaryote or a plant or algal cell compared to the amount typically present in wild-type results in incomplete division or no division of the prokaryote or plastid(s) in the plant or algal cell. As an illustrative

¹ (Emphasis added) Specification, page 15, lines 11-24; page 44, line 20 to page 45, line 3.

but non-limiting example, in photosynthetic prokaryotes such as cyanobacteria, a decreased amount of Ftn2 polypeptide can result in long filamentous cells, up to many times longer than a wild-type cell. As an illustrative but non-limiting example, in plants such as Arabidopsis, a decreased amount of Ftn2 polypeptide can result in a single or a few very large chloroplasts present in a single leaf mesophyll cell.”²

New Claims 47-49 and 52-54 are supported by the above disclosure with respect to the recited percent identity of Claim 43.

In addition, the recital in new Claims 47 and 52 of amino acids 86-509 (at the N-terminal end) and 683-793 (at the C-terminal end) of SEQ ID NO:2, respectively, is shown in Figure 3B and the Specification’s teaching that Figure 3B

“shows the putative **functional** and conserved protein domain, which are depicted as wider black boxes; their numerical positions within the AtFtn2 sequence are also indicated. Black lines above the diagram delineate regions of AtFtn2 **conserved** among Ftn2 homologues (see Figures 4-6).”³

New Claims 48 and 53 are further supported by the following disclosure with respect to the DnaJ domain from amino acid 89 to amino acid 153 of SEQ ID NO:2:

“A search for protein motifs with InterProScan revealed a putative DnaJ domain (AtFtn2 residues **89-153**), InterPro accession IPR001623, Pfam conserved domain pfam00226.”⁴

New Claims 44 and 45 have the same support as pending Claim 26.

New Claim 46 has the same support as pending Claim 29.

New Claims 50 and 55 have the same support as pending Claim 24.

Claim amendments were made to describe particular embodiments of the invention, notwithstanding Applicants’ belief that the cancelled and unamended claims would have been allowable, without acquiescing to any of the Examiner’s arguments, and without waiving the right to prosecute the unamended (or similar) claims in another application, but rather for the

² Specification, page 15, lines 2-10.

³ (Emphasis added) Specification, page 11, lines 27-30.

⁴ Specification page 90, lines 12-13 and Figure 3B. The Specification, page 44, lines 6-7, also teaches that “In some embodiments, in both photosynthetic prokaryotes and plants, the Ftn2 polypeptide is contemplated to possess a DnaJ domain.”

purpose of furthering Applicants' business goals and expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG).⁵

2. **WITHDRAWAL OF CLAIMS 23-42**

Applicants note the Examiner's withdrawal of Claims 23-42.⁶

3. **WITHDRAWN REJECTIONS**

Applicants note, with appreciation, that the Examiner withdrew the following prior rejections:⁷

- A. Rejection of Claims 23-26 under 35 U.S.C. § 112, first paragraph (written description), and
- B. Rejection of Claim 29 under 35 U.S.C. § 112, second paragraph (indefiniteness).

1. **REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)**

The Examiner rejected Claims 23-34 under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement.⁸ Applicants respectfully traverse because both the Specification and prior art provide the requisite enablement. The Examiner had different arguments with regards to the "Arabidopsis . . . Ftn2 protein" of Claims 23-30 and to "SEQ ID NO:2" of Claims 31-34. These arguments are addressed separately below, in addition to the enablement of new Claims 43-55.

A. **Arabidopsis "Ftn2 protein" In Claims 23-30**

The Examiner argued that "the specification fails to teach how to make the full scope of Arabidopsis nucleic acids encoding an Ftn2 protein."⁹ This rejection is moot in view of the cancellation of this term and replacement with the term "SEQ ID NO:3."

B. **"SEQ ID NO:2" In Amended Claims 31-34**

The Examiner's position with respect to enablement of SEQ ID NO:2 is unclear. On one hand, the Examiner recognized that the Specification is "enabling for a nucleic acid encoding

⁵ 65 Fed. Reg. 54603 (September 8, 2000).

⁶ Office Action, page 2, item 2.

⁷ Office Action, page 3, items 5 and 6.

⁸ Office Action, page 3, item 7.

⁹ Office Action, page 6, second paragraph.

SEQ ID NO:2.”¹⁰ However, the Examiner advanced a contradictory statement that “while the specification is enabled for **making** a nucleic acid encoding SEQ ID NO:2, it does not teach **how to use** a plant transformed with a nucleic acid that encodes it.”¹¹ In the same vein, the Examiner stated that the “specification also does not teach **how to use** plants in which Ftn2 is overexpressed”¹² and that “[p]lants in which Ftn2 is overexpressed would have a large number of small chloroplasts. How does one **use** such plants?”¹³

To expedite prosecution, Applicants assume that the Examiner’s position is that the Specification allegedly does not teach “how to use” the claimed invention, and aver that both the Specification and prior art teach uses of the claimed vectors that are within the ordinary skill in the art, as discussed below.

i. The Specification Teaches Methods of Using The Recited Compositions

The Examiner is respectfully reminded that

“the law makes clear that the specification need teach only one mode of making and using a claimed composition.”¹⁴

The specification teaches not just one, but several uses for vectors that comprise the nucleic acid sequence SEQ ID NO:3 (Claims 23-30) that encodes the amino acid sequence SEQ ID NO:2 (Claims 31-34), and that are within the ordinary skill in the art. More particularly, the Specification teaches that expression of Ftn2 proteins (such as the recited SEQ ID NO:2) would “result in **changes** in plastid size, shape and/or number.”¹⁵ In other words, the “change” can be either an **increase** or **decrease** in plastid size, shape and/or number. Under the law, all that is required is that the Specification teaches **one** use, *i.e.*, how to use cells containing **either** an increase or a decrease in plastid size, shape

¹⁰ Office Action, page 3, item 7.

¹¹ (Emphasis added) Office Action, page 5, last full paragraph.

¹² (Emphasis added) Office Action, page 5, 1st full paragraph.

¹³ (Emphasis added) Office Action, page 6, 6th paragraph.

¹⁴ *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003), citing *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69 (D. Mass. 2001).

¹⁵ (Emphasis added) Specification, page 79, lines 10-17.

and/or number. The specification does more by teaching several applications of these changes in plants, protists, bacteria, and other organisms.

For example, in plant cells, the Specification teaches that these changes may be **used** to “to vary agronomic and horticultural characteristics of economically important plants, such as crop, ornamental, and woody plants.”¹⁶ Such **uses** include producing “improved productivity and/or increased vigor due to enhanced photosynthetic capacity, and/or to allow enhanced production of commercially important compounds that accumulate in plastids either naturally or as a result of genetic engineering. Examples of compounds that naturally accumulate in plastids include vitamin E, pro-vitamin A, essential (aromatic) amino acids, pigments (carotenes, xanthophylls, chlorophylls), starch, and lipids. Plants with altered plastid size or number have further applications in improving the efficiency of plastid transformation technologies that are **used** for the introduction of transgenes into the plastid genome.”¹⁷ Additional **uses** taught by the Specification also include testing the suitability of the plastid division genes as herbicide targets,¹⁸ and regulation of morphogenesis of plant chloroplasts.¹⁹

In protists, the Specification teaches that the invention’s vectors may be **used** to test the suitability of the plastid division genes as targets for controlling growth of parasitic protists such as the malarial protist *Plasmodium falciparum* and *Toxoplasma gondii*.²⁰

In bacteria, the artisan learns from the Specification that **uses** of the invention’s vectors include controlling bacterial growth in fermenters.²¹

Since the Specification teaches not just one, but several uses for the claimed vectors, Claims 23-34 are enabled.

The Examiner is respectfully reminded that

“If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently

¹⁶ Specification, page 5, lines 18-20.

¹⁷ Specification, page 79, lines 18-27.

¹⁸ Specification, page 83, lines 2-3.

¹⁹ Specification, page 37, line 29 to page 38, line3.

²⁰ Specification, page 52, lines 17-23.

²¹ Specification, page 37, line 29 to page 38, line3.

supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.”²²

Therefore, should the claims continue to be rejected for alleged non-enablement, Applicants respectfully request the Examiner to provide an explanation, supported by evidence, with respect to **each** disclosed use.

**ii. The Prior Art Teaches Methods of Using Vectors That Express
Proteins Involved In Plastid Division**

The Examiner is directed by the MPEP that

“If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. 112, first paragraph.”²³

The Specification teaches that the recited SEQ ID NO:3 encodes SEQ ID NO:2, which is “involved in plastid division and morphology.”²⁴ The prior art teaches that proteins that are involved in plastid division, such as FtsZ proteins (Osteryoung²⁵ at Tab 1, and Hitz et al.²⁶ at Tab 2) that are expressed by vectors may be “**used** to immunize animals to produce polyclonal or monoclonal antibodies with specificity for peptides or proteins comprising the amino acid sequences. These antibodies can then be used to screen cDNA expression libraries to isolate full-length cDNA clones of interest.”²⁷ In addition, the antibodies “**are useful** for detecting the polypeptides of the instant invention in situ in cells or in vitro in cell extracts.”²⁸

In the case where expression of a plastid division protein results in transgenic plants that have “a novel phenotype with advantageous qualities, including increased numbers of chloroplasts,”²⁹ these plants are **useful** for increasing the nutritional quality³⁰ and viability³¹ of

²² MPEP 2164.01(c)

²³ MPEP 2164.01(c).

²⁴ Specification, page 35, lines 29-30.

²⁵ Osteryoung, U.S. Patent No. 5,981,836, filed June 26, 1997, issued Nov. 9, 1999.

²⁶ Hitz et al., U.S. Patent No. 6,812,382, filed Feb. 9, 2000, issued Nov. 2, 2004.

²⁷ (Emphasis added) Hitz et al., column 12, lines 1-9.

²⁸ (Emphasis added) Hitz et al., column 13, lines 45-62.

²⁹ Osteryoung, column 2, lines 26-29.

³⁰ Osteryoung, column 1, lines 54-59.

plants because “[p]lastids are the site of the synthesis of essential amino acids, vitamin E, pro-vitamin A, starch, certain growth hormones, lipids, and pigments such as carotenes, xanthophylls, and chlorophylls.”³² Yet another **use** involves “regulating the division of other plastids, including chromoplasts, amyloplasts, and elaioplasts. These plastids are of great agronomic importance because they synthesize carotenoids, starch, and oils, respectively.”³³ In other words, increasing the size and/or number of chloroplasts has the above uses. This satisfies enablement.

As discussed above, should the claims continue to be rejected for alleged non-enablement, Applicants respectfully request the Examiner to provide an explanation, supported by evidence, with respect to **each** of the above uses taught by the prior art, as required by MPEP 2164.01(c).

iii. Expression of SEQ ID NO:2 Increases The size and/or reduces the number of chloroplasts

The enclosed reference by Viitha et al. (Tab 3)³⁴ demonstrates that overexpression of Arc6 (SEQ ID NO:2) results in plants with enlarged and/or reduced number of chloroplasts.³⁵ Both of these **morphological changes** and their **uses** are taught in the Specification, as discussed above. This is further evidence of enablement of the recited vectors.

Since both the Specification and the prior art provide more than adequate teaching of methods how to use the recited vectors, Applicants respectfully request withdrawal of the rejection of Claims 23-34 under 35 U.S.C. 112, first paragraph.

C. New Claims 43-55

New Claims 43-55 recite both structure (percent identity to SEQ ID NO:2) and function (plastid division in Claims 43-50 and prokaryote cell division in Claims 51-55). The amino acids recited in the claims may be identified by searching electronic sequence databases, as taught by

³¹ Osteryoung, column 2, lines 63-65.

³² Osteryoung, column 2, lines 60-63.

³³ Osteryoung, column 6, lines 33-45.

³⁴ Viitha et al. (August 2003) “ARC6 is a J-Domain Plastid Division Protein And An Evolutionary Descendant Of The Cyanobacterial Cell Division Protein Ftn2,” The Plant Cell 15:1918-1933.

the Specification in Example 3, in which a tblastn search identified 57 sequences from 31 species of plants, moss, fern and cyanobacteria.³⁶ Once identified, these sequences may be **made**³⁷ by expression in vectors, and **used** as described above, including in the transformation of cells and regeneration of plants,³⁸ as taught by the Specification. Thus, new Claims 43-55 are enabled.

1. **REJECTION OF CLAIMS 23-26 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)**

The Examiner rejected Claims 23-26 under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description support.³⁹ This is addressed below with respect to the rejected and new claims.

A. Rejected Claims 23-26

The rejection is moot in view of the amendment of Claims 23-26 to recite “SEQ ID NO:3.” Therefore, Applicants respectfully request that the Examiner withdraw this rejection.

B. New Claims 43-55

To expedite prosecution, Applicants address the Examiner’s arguments as they may arguably apply to new Claims 43-55. The written description requirement is satisfied if the disclosure by Applicant

“convey[s] with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.”⁴⁰

The Examiner contended that “[t]here is no description of the structure required for the recited function, and no description of the necessary and sufficient structural elements of a protein with Ftn2 function.”⁴¹ This statement is inaccurate. The Specification describes that common

³⁵ Vitha et al., page 1923, 2nd column to page 1925 2nd column, and Table 3.

³⁶ Specification, page 92-95.

³⁷ Specification, page 71-78.

³⁸ Specification, page 78-79

³⁹ Specification, page 6, item 5.

⁴⁰ *In re Alton*, 37 USPQ2d 1578 (Fed. Cir. 1996), citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

⁴¹ Office Action, page 7, 5th paragraph.

attributes of the genus include amino acids 86-509 (at the N-terminal end) and 683-793 (at the C-terminal end) as shown in Figure 3B and the Specification's teaching that Figure 3B

"shows the putative **functional** and conserved protein domain, which are depicted as wider black boxes; their numerical positions within the AtFtn2 sequence are also indicated. Black lines above the diagram delineate regions of AtFtn2 conserved among Ftn2 homologues (see Figures 4-6)."⁴²

The features relating to amino acids 86-509 (at the N-terminal end) and 683-793 (at the C-terminal end) are recited in new Claims 44 and 46, respectively. Thus, Claims 44 and 46 have sufficient written description.

The Specification further teaches the conservation, within the above-discussed amino acids 86-509, of a non-canonical DnaJ domain (amino acids 89-153) that lacks the central HPD motif, as follows:

"A search for protein motifs with InterProScan revealed a putative DnaJ domain (AtFtn2 residues 89-153), InterPro accession IPR001623, Pfam conserved domain pfam00226. However, ClustalW alignment of this domain with all predicted DnaJ domains from the Pfam database (277 sequences) revealed that the central Histidine-Proline-Aspartate (HPD) motif typical for DnaJ proteins is not present in *AtFtn2* or in other plant and cyanobacterial *Ftn2* homologues (Figure 4)."⁴³

The feature relating to the DnaJ domain (amino acids 89-153) in the N-terminal end of the protein is recited in new Claim 45. Therefore, new Claim 45 has the requisite written description.

The Examiner also argued that "[t]he only species described in the specification are SEQ ID NO:3 from *A. thaliana*. The sequences from other species are not described."⁴⁴ This is incorrect. The Specification⁴⁵ describes protein sequences that have the recited percent identity to SEQ ID NO:2, and that are derived from **twelve different species**, as follows:

⁴² (Emphasis added) Specification, page 11, lines 27-30.

⁴³ Specification page 90, lines 12-13 and Figure 3B. The Specification, page 44, lines 6-7, also teaches that "In some embodiments, in both photosynthetic prokaryotes and plants, the Ftn2 polypeptide is contemplated to possess a DnaJ domain."

⁴⁴ Office Action, page 7, last full paragraph. See also the statement that "Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO:3 is insufficient to describe the claimed genus." Office Action, page 8, 1st paragraph.

⁴⁵ Specification, Table 3, page 92.

Species	ORF/Gene name	Accession # (DNA)	Protein Accession #	Type ²
<i>Oryza sativa</i>		BK000999		cDNA
<i>Protochlorococcus marinus</i> MED4	Contig1, Gene 533 ¹			Gen
<i>Protochlorococcus marinus</i> MT9313	Contig1, gene2677 ²			Gen
<i>Synechococcus</i> sp. PCC 7002	Contig05130 2-306 ³			Gen
<i>Synechococcus</i> sp. PCC 7942	<i>Ftn2</i>	AF421196	AAL16071	Gen
<i>Anabena</i> PCC 7120	all2707	AP003590 ⁴ NC 003272 ⁵	BAB74406 NP 486747	Gen
<i>Nostoc punctiforme</i> ATCC 29133	Contig493 Gene 84 ⁶			Gen
<i>Synechocystis</i> sp. PCC 6803	sl10169	NC_000911 ⁷ D63999 ⁸	NP_441990 BAA10060	Gen
<i>Synechococcus</i> sp. WH8102	Gene 3082			
<i>Thermosynechococcus elongatus</i> BP-1	tlr0758			Gen
<i>Trichodesmium erythraeum</i> IMS101	Contig97 Gene 8639			Gen
<i>Chlamydomonas reinhardtii</i>	genie.294.6 (Scaffold294, nt 47288-51078)			Gen

¹ Draft analysis http://genome.ornl.gov/microbial/pmar_med/² Draft analysis http://genome.ornl.gov/microbial/pmar_mit/³ Unfinished fragment of the genome, Joint Genome Institute (JGI)⁴ Complement (211130..213526)⁵ Complement (3300430..3302826)⁶ Draft analysis; <http://genome.ornl.gov/microbial/npun/31may01/npun.html>⁷ Complement (2314780..2316924)⁸ Complement (47521..49665)

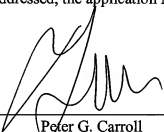
Each of the sequences in the above Table is **known**, since it is either listed in GenBank or available online. Since the Court has held that “satisfaction of the written description requirement does not require either the recitation or incorporation by reference of [known] genes

and sequences,⁴⁶ the above disclosure in the Specification of 12 sequences that fall within the scope of the claimed vectors amply satisfies the written description requirement of new Claims 43-55.

CONCLUSION

All grounds of rejection having been addressed, the application is in condition for allowance.

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⁴⁶ *Falkner v. Inglis*, 448 F.3d 1357, 79 USPQ2d 1001 (Fed. Cir. 2006)